

mode chip designed in 130 nm CMOS technology [1]. We present results of a PET-ToF demonstrator scanner based on this ASIC and featuring a highly integrated readout and DAQ system.

The Detector Module is composed of 8 matrices of 4x4 LYSO scintillating crystals, each with a size of 3.1 x 3.1 x 15 mm<sup>3</sup>. These matrices are optically coupled to 8 arrays of Hamamatsu TSV-MPPCs. The crystal matrices and associated MPPCs plug directly in the Frontend Boards forming a compact detecting unit with active area 59x29 mm<sup>2</sup>. The present results were obtained with a partially assembled ring (16 Modules) corresponding to 2048 SiPM readout channels.

The Frontend board integrates two ASICs allowing the readout and digitization of 128 MPPC pixels. On-chip TDCs produce two time measurements allowing the determination of the event time and of the time-over-threshold. A Concentrator board reads the data from eight Frontend boards (1024 channels) and transmits assembled data frames through a serial link to the PCIe based DAQ board in the data acquisition PC.

At present the PET-ToF demonstrator is fully assembled and in operation (Figure 1). We will report on the detector performance, including energy resolution, spatial resolution, time resolution and rate performance of the system. Images with phantoms will also be presented.

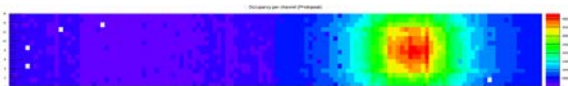


Figure 1 - Flood histogram of the full scanner obtained with a Na22 point source.

#### References:

[1] M.D. Rolo, R. Bugalho, F. Goncalves, G. Mazza, A. Rivetti, J.C. Silva, R. Silva, and J. Varela. TOPPET ASIC for PET applications. *Journal of Instrumentation*, 8(02):C02050, 2013.

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#### Novel anti-tumour agents targeting the cell membrane

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The cell membrane not only functions as a physical barrier between the intracellular and extracellular space, it harbors critical components involved in receptor-ligand interactions, signal transduction and drug uptake. Targeting the cell membrane represents a novel strategy to improve anti-cancer therapy. Our work focuses on two different approaches. The first involves lipid rafts. These are dynamic, cholesterol/sphingolipid-enriched microdomains within biological membranes, and play a crucial role in the induction of (apoptotic) cell death by radiation, pro-apoptotic receptor agonists and synthetic alkyl-phospholipids.

The second approach addresses insufficient drug delivery into tumor cells, which represents a major limitation of cytostatic therapy. We found that co-formulation and co-administration of liposome-encapsulated chemotherapy and synthetic short-chain sphingolipids (SCS) improves drug availability by enhancing intracellular drug uptake. Specific biophysical requirements of both the SCS (chain length and polarity) and chemotherapeutic agent (amphiphilicity) determine the optimal conditions for improved drug delivery. Doxorubicine and mitoxantrone are two frequently prescribed chemotherapeutic agents that benefit from this cell membrane-targeting approach. In vitro and in vivo studies demonstrate higher drug efficacy and/or lower toxicity in relevant tumor model systems. Mechanistic analyses demonstrate that SCS preferentially insert into tumor cell membranes enhancing the intrinsic capacity to translocate amphiphilic drugs.

**Keywords:** cell membrane, sphingolipids, liposomes

#### References:

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#### Assessment of MicroDiamond PTW 60019 detector and its use in small radiosurgery fields of Leksell Gamma Knife

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**Purpose:** Modern radiotherapy is based on using small radiation fields and their segments. For clinical use they need to be verified by measurement. But measurement of small radiosurgery fields is very problematic task because of dosimetry challenges, such as loss of charged particle equilibrium, accurate positioning of detector and its small size. Purpose of this study is to assess new synthetic single crystal MicroDiamond PTW 60019 detector. Its dosimetry characteristics from the manufacturer and especially small size of its sensitive volume (0.004 mm<sup>3</sup>) make the detector promising tool for this task.

**Materials and Method:** In this study basic dosimetry characteristics of MicroDiamond detector were verified in clinical linear accelerator photon and electron beams. Measurements involved short time stability and detector response dependence on dose rate, beam energy, temperature and angular dependence. In addition, measurement of relative output factors for Leksell Gamma Knife Perfexion was performed in order to test dosimeter performance for small fields. Collimator sizes 4 mm, 8 mm and 16 mm were used. Results obtained by this detector were compared with ELEKTA reference values and independent Monte Carlo Geant4 simulation.

**Results:** Stabilization of detector response was always performed before starting measurement. For this purpose 40 minutes irradiation in reference conditions was necessary (corresponding delivered dose was about 100 Gy). After this time the response was relatively stable with difference between maximum and minimum value 0.25% and standard deviation of all measurements 0.07% within an hour (normalized for this and all subsequent measurements to mean value of response). Dose rate dependence was measured for 6 different dose rates. Difference between maximum and minimum value was 0.24%. Energy dependence of detector was performed for 2 photon energies (6 and 18 MV) and 5 electron energies (6-20 MeV). Difference between maximum and minimum photon beam values was 0.12%, for electron beams this difference was 4.54% with standard deviation of response values 1.62%. Results for temperature and angular dependence are not finalized yet. Finally, results of comparative measurement for relative output factors of the Leksell Gamma Knife for 4 and 8 mm collimators were 0.831 and 0.900, respectively. These values are in a good agreement with vendor values (0.814 and 0.900) and Monte Carlo simulation.

**Conclusion:** New MicroDiamond PTW 60019 detector appears to be a promising detector for relative output factor measurements in small radiosurgery fields. Verified dosimetric properties of the detector are in limits set by manufacturer. However, relatively long pre-irradiation process is necessary prior to measurement before the detector can produce reliable data. Further measurements will follow. This work was supported by CTU grant no. SGS15/217/OHK4/3T/14.

**Keywords:** MicroDiamond, small field dosimetry

#### References:

<http://www.ptw.de/2732.html>

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# **ENTERVISION biological dosimetric phantom. Proof of concept and results**

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Development of clinical treatment protocols for radiation therapy is dependent on the availability of information on the biological efficacy of radiation doses. In order to gain robust data, multiple cell irradiation experiments must be performed at different dose points, using a range of cell lines. Therefore, it is important to be able to verify the biological effects of complex dose distributions in homeomorphic phantoms, alongside measurements of physical dose. One of the ENTERVISION projects focuses on the development of a biological dosimetric phantom. Firstly, the phantom and desired set-ups were evaluated then its suitability for radiobiology studies were assessed during a set of cell irradiations. Status: The phantom was irradiated mimicking the patients' pathway starting with the CT scan, followed by treatment planning and being irradiated. For the irradiation, an uniform dose distribution was delivered with a proton beam and the process was repeated using a carbon ion beam. The dose was measured from pinpoint ionisation chambers readings and the uniformity was assessed with radiochromic films. The experimental results were compared with the TPS and Monte Carlo calculations. Using MC simulations it was also investigated how the simulation of a more detailed geometry would affect the obtained results. From the radiobiology studies the cell survival by analyzing its proliferation was studied. Results: The calculated mean deviation was below 2% for both beams used. This brings the result within the acceptance threshold as desired by CNAO QA procedures. Conclusion: The experimental results obtained showed good agreement with both TPS and Monte Carlo simulations. And the radiobiological results showed the possibility of multi-variable analysis (LET and Dose) that is available to be done with the ENTERVISION Phantom.

**Keywords:** LET, RBE, Radiobiology,

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## **Evaluation of Patients Dose in PET Studies from CT Contrast Agents**

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**Introduction:** The increased availability of PET-CT devices in addition to the interchange of people and technology between nuclear medicine and radiology explains the increased use of CT techniques like enhanced contrast CT in nuclear medicine. The benefits of the use of contrast agents, especially in terms of the increased accuracy, for enhancing different image modalities are understood and well discussed in the literature. On the other hand, in terms of evaluating the different side effects from the use of these contrast agents only the visible and short-term reactions have been discussed. In respect to studying for a possible increase in dose exposure from the interaction of the radiopharmaceutical radiation with the contrast agent in a contrast enhanced PET-CT study and its effect in the patient radiation exposure is yet to be investigated.

**Materials and Methods:** This study is aimed to investigate the dose deposition differences with respect to the nuclear medicine isotope radiation interaction with the high density

and atomic number of the contrast agent due to increased absorption and scatter of the internal radiation in the patients' tissue. This has been performed with the use of Monte Carlo simulations of 10 patient studies where contrast agent had been used.

**Results:** Preliminary results show an increase in the dose deposition in the regions enhanced by contrast and its surroundings.

**Conclusion:** Further quantification of this increased dose deposition in different organs at risk and its estimated effect will be presented.

**Keywords:** PET-CT, Nuclear Medicine, Patient dose

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## **Proton radiotherapy at PTC Czech in Prague**

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**Purpose:** In the last two decades, particle therapy is slowly spreading from complementary programs of research institutions to dedicated healthcare facilities. Together with this evolution, particle therapy is refocusing from passive modes to the active pencil beam scanning mode (PBS). Higher degree of freedom, in sense of treatment conformity in PBS, is followed by more extensive demands in patient geometry determination. PTC Czech in Prague launched in December 2012 in PBS and it is the only mode of proton beam delivery currently used for patient treatment. The use of PBS technique raised new challenges such as plan robustness during the treatment course and mitigation of breathing motion influence on PBS treatment field delivery. The purpose of this poster is to demonstrate some of motion management studies conducted in the course of preparation for lung/breast lesions treatment.

**Materials and Methods:** A study with "MartiXX phantom" simulating breathing movement was conducted in order to examine the use of the repainting technique combined with respiratory gating. The goal was to evaluate the benefit of this combination for dose distribution delivery robustness against prolonged treatment time in the case of repainting itself. In another study, four Hodgkin's lymphoma patients, where respiratory gating system (Dyn'R) was applied, were examined. The inter-fractional movement of diaphragm on their setup X-ray images was evaluated. For the evaluation a script for edge detection using ITKsnap library was created. The error of this method was 1 mm.

**Results:** The evaluation of the "MartiXX phantom" experiment demonstrated significant mitigation of breathing motion when respiratory gating was applied. In this case, the treatment time was increased by 98 %. The use of gating combined with 5 times repainting demonstrated only mild improvement in movement mitigation compared to gating only case at cost of 233 % time increase. The degree of the dose distribution delivery improvement was evaluated through gamma analysis of dose planes acquired with MartiXX detector for dynamic and static case.

The evaluation of the diaphragm movement showed for 3 patients the difference trespassing the 5 mm threshold in 2-3 setups out of 7-11 of total, while in the case of the fourth patient all deviations were beneath 4 mm.

**Conclusions:** The selected studies for this poster suggest a strong benefit of respiratory gating. Additional mitigation technique like repainting might improve the outcome of dose delivery, but at a high treatment time cost. Nevertheless, the choice of the mitigation strategy should be always verified with a PET-QA in order to adopt the strategy if needed. Further, the evaluation of diaphragm position reproducibility gives some encouraging results although there are some papers [6] claiming low correlation of tumor lesion and diaphragm position.

**Keywords:** Motion management